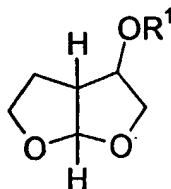


Claims

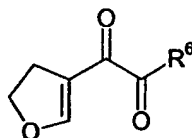
1. A process for the preparation of compounds of formula (I)



(I)

diastereoisomers, enantiomers, and mixtures thereof,
wherein R¹ is hydrogen, comprising:

- a) treating a compound of formula (XII)



(XII)

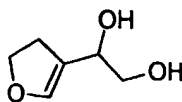
wherein:

R⁶ is halogen, -OR⁷, or -NR⁸R⁹;

R⁷ is hydrogen, C₁₋₆alkyl, C₃₋₈cycloalkyl, C₆₋₁₄aryl, or C₆₋₁₄arylC₁₋₆alkyl;

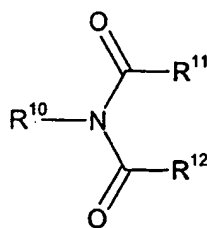
R⁸ and R⁹ are independently selected from hydrogen, C₁₋₆alkyl, C₃₋₈cycloalkyl, C₆₋₁₄aryl, and C₆₋₁₄arylC₁₋₆alkyl;

with a first reducing agent to form an alcohol of formula (III)



(III)

- b) treating the alcohol with bromine, iodine, iodine monochloride, an N-fluoro bis sulfonamide or a compound of formula (XIII)



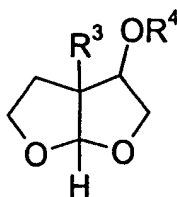
(XIII)

wherein:

R^{10} is chlorine, bromine, or iodine; and

R^{11} and R^{12} are independently selected from C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl, or R^{11} and R^{12} together with the atoms to which they are attached form a 5-8 membered ring;

to form a compound of formula (II)



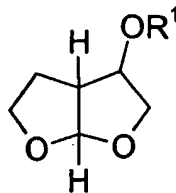
(II)

wherein R^3 is halogen, and R^4 is hydrogen; and

c) treating a compound of formula (II) with a second reducing agent to afford a compound of formula (I), wherein R^1 is hydrogen.

2. A process for the preparation of compounds of formula (I) according to claim 1, wherein said first reducing agent is selected from the group consisting of diisobutylaluminum hydride (DIBAL), sodium borohydride, and lithium aluminum hydride, R^6 in the compound of formula (XII) is $-OR^7$ wherein R^7 is C_{1-6} alkyl, the compound of formula (XIII) is N-bromosuccinimide, and the second reducing agent is palladium on carbon in combination with hydrogen.

3. A process for the preparation of compounds of formula (I)

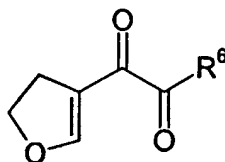


(I)

diastereoisomers, enantiomers, and mixtures thereof,

wherein R^1 is $-C(O)R^2$; and R^2 is C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl, comprising:

- a) treating a compound of formula (XII)



(XII)

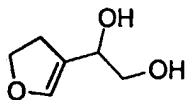
wherein:

R^6 is halogen, $-OR^7$, or $-NR^8R^9$;

R^7 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl; and

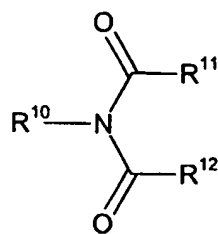
R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl;

with a first reducing agent to form an alcohol of formula (III)



(III)

- b) treating the alcohol with bromine, iodine, iodine monochloride, an N-fluoro bis sulfonamide or a compound of formula (XIII)



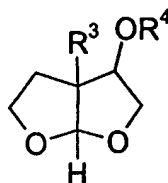
(XIII)

wherein:

R^{10} is chlorine, bromine, or iodine; and

R^{11} and R^{12} are independently selected from C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl, or R^{11} and R^{12} together with the atoms to which they are attached form a 5-8 membered ring;

to form a compound of formula (II)



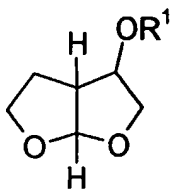
(II)

wherein R^3 is halogen, and R^4 is hydrogen;

c) treating a compound of formula (II) with a second reducing agent to afford a compound of formula (I), wherein R^1 is hydrogen; and

d) resolving to form a compound of formula (I), wherein R^1 is $-C(O)R^2$ and R^2 is C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl.

4. A process for the preparation of compounds of formula (I)

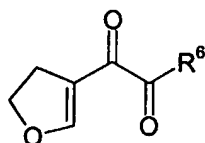


(I)

diastereoisomers, enantiomers, and mixtures thereof,

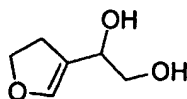
wherein R^1 is hydrogen or $-C(O)R^2$ wherein R^2 is C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl,

comprising reducing a compound of formula (XII)



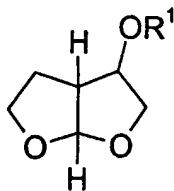
(XII)

to afford an alcohol of formula III



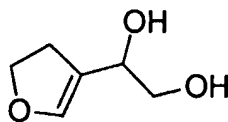
(III).

5. A process for the preparation of compounds of formula (I)



wherein R^1 is hydrogen,

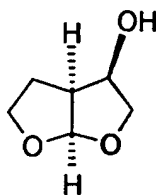
comprising treating a compound of formula (III)



(III)

with an acid selected from the group consisting of hydrochloric acid, hydrobromic acid, hydroiodic acid, acetic acid, sulfuric acid, and sulfonic acid.

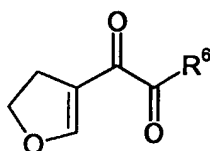
6. A process for the preparation of a compound of formula (V)



(V)

substantially free from other diastereoisomers, comprising:

a) treating a compound of formula (XII)



(XII)

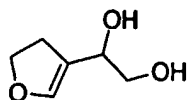
wherein:

R^6 is halogen, $-OR^7$, or $-NR^8R^9$;

R^7 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl; and

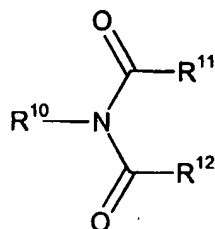
R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl;

with a first reducing agent to form an alcohol of formula (III)



(III)

b) treating the alcohol with bromine, iodine, iodine monochloride, an N-fluoro bis sulfonamide or a compound of formula (XIII)



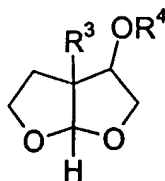
(XIII)

wherein:

R^{10} is chlorine, bromine, or iodine; and

R^{11} and R^{12} are independently selected from C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl, or R^{11} and R^{12} together with the atoms to which they are attached form a 5-8 membered ring;

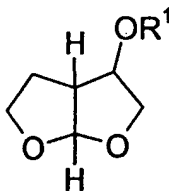
to form a compound of formula (II)



(II)

wherein R^3 is halogen and R^4 is hydrogen;

c) treating a compound of formula (II) with a second reducing agent to afford a compound of formula (I)

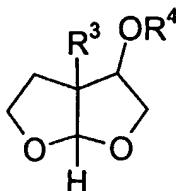


(I)

wherein R^1 is hydrogen; and

d) resolving to form a compound of formula (I), wherein R^1 is hydrogen or $-C(O)R^2$ and R^2 is C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl.

7. A compound of formula (II)



(II)

wherein:

R^3 is halogen;

R^4 is hydrogen or $-C(O)R^5$;

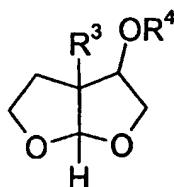
R^5 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl; and diastereoisomers, enantiomers, and mixtures thereof.

8. A compound of formula (II) according to claim 7 wherein R^3 is bromine and R^4 is hydrogen.

9. A compound of formula (II) according to claim 7 wherein R^3 is bromine, R^4 is $-C(O)R^5$ and R^5 is C_{1-6} alkyl,

10. A compound of formula (II) according to claim 7 wherein R^3 is bromine, R^4 is $-C(O)R^5$, and R^5 is $-CH_3$.

11. A process for the preparation of compounds of formula (II)



(II)

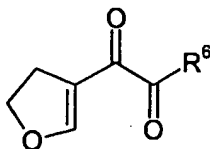
wherein:

R^3 is halogen;

R^4 is hydrogen or $-C(O)R^5$;

R^5 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl; and diastereoisomers, enantiomers, and mixtures thereof, comprising:

a) treating a compound of formula (XII)



(XII)

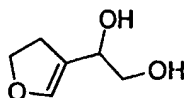
wherein:

R^6 is halogen, $-OR^7$, or $-NR^8R^9$;

R^7 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl; and

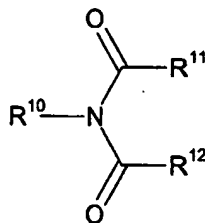
R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl;

with a reducing agent to form an alcohol of formula (III)



(III)

b) treating said alcohol with bromine, iodine, iodine monochloride, an N-fluoro bis sulfonamide or a compound of formula (XIII)



(XIII)

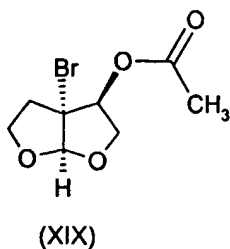
wherein:

R^{10} is chlorine, bromine, or iodine; and

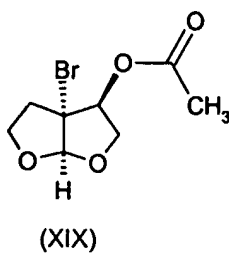
R^{11} and R^{12} are independently selected from C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl, or R^{11} and R^{12} together with the atoms to which they are attached form a 5-8 membered ring; to form a compound of formula (II), wherein R^3 is halogen and R^4 is hydrogen; and

c) resolving to yield a compound of formula (II) wherein R^3 is halogen; R^4 is hydrogen or $-C(O)R^5$; and R^5 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl.

12. A compound of formula (XIX)

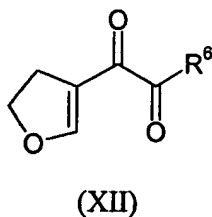


13. A process for the preparation of a compound of formula (XIX)



comprising:

a) treating a compound of formula (XII)



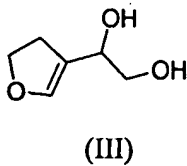
wherein:

R⁶ is halogen, -OR⁷, or -NR⁸R⁹;

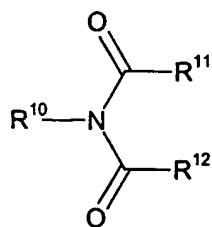
R⁷ is hydrogen, C₁₋₆alkyl, C₃₋₈cycloalkyl, C₆₋₁₄aryl, or C₆₋₁₄arylC₁₋₆alkyl; and

R⁸ and R⁹ are independently selected from hydrogen, C₁₋₆alkyl, C₃₋₈cycloalkyl, C₆₋₁₄aryl, and C₆₋₁₄arylC₁₋₆alkyl;

with a reducing agent to form an alcohol of formula (III)



b) treating said alcohol with bromine, iodine, iodine monochloride, an N-fluoro bis sulfonamide or a compound of formula (XIII)



(XIII)

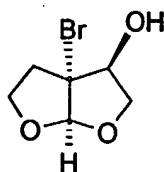
wherein:

R^{10} is chlorine, bromine, or iodine; and

R^{11} and R^{12} are independently selected from C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl, or R^{11} and R^{12} together with the atoms to which they are attached form a 5-8 membered ring; and

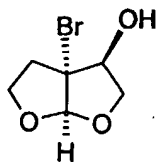
c) optionally resolving to yield a compound of formula (XIX).

14. A compound of formula (XX)



(XX)

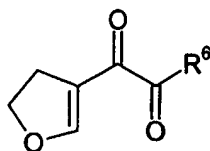
15. A process for the preparation of a compound of formula (XX)



(XX)

comprising:

a) treating a compound of formula (XII)



(XII)

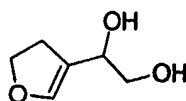
wherein:

R^6 is halogen, $-OR^7$, or $-NR^8R^9$;

R^7 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl; and

R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl;

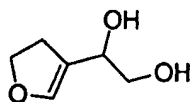
with a reducing agent to form an alcohol of formula (III)



(III)

- b) treating said alcohol with N-bromosuccinimide to form a compound of formula (XX); and
- c) optionally resolving to yield diastereoisomers of compounds of formula (XX).

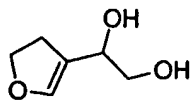
16. A compound of formula (III)



(III) .

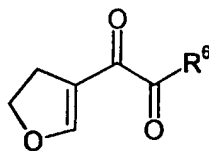
17. 1-(4,5-dihydrofuran-3-yl)ethane-1,2-diol.

18. A process for the preparation of compound (III)



(III)

comprising treating a compound of formula (XII)



(XII)

wherein R^6 is halogen, $-OR^7$, or $-NR^8R^9$; where R^7 is hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, or C_{6-14} aryl C_{1-6} alkyl; and R^8 and R^9 are independently selected from hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-14} aryl, and C_{6-14} aryl C_{1-6} alkyl; with a reducing agent.

19. A process according to claim 18 wherein the reducing agent is selected from the group consisting of di-*isobutyl*aluminum hydride (DIBAL), sodium borohydride, and lithium aluminum hydride.

20. A process for the preparation of compounds of formula I, II, V, XIV, XIX, and XX, according to any of claims 1, 3, 4, 6, 11, 13, or 15 wherein the first reducing agent is selected from the group consisting of di-*isobutyl*aluminum hydride (DIBAL), sodium borohydride, and lithium aluminum hydride, wherein R^6 in the compound of formula (XII) is $-OR^7$ where R^7 is C_{1-6} alkyl, wherein the compound of formula (XIII) is N-bromosuccinimide, and the second reducing agent is palladium on carbon in combination with hydrogen.

21. A process according to any of claims 1, 2, 3, or 4 further comprising the step of resolving to obtain single enantiomers.